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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,574	04/03/2001	Victor I. Lyamichev	FORS-06137	2434

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EXAMINER	
GUNTER, DAVID R	
ART UNIT	PAPER NUMBER
1634	7

DATE MAILED: 05/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/825,574	Applicant(s) LYAMICHEV ET AL.	
	Examiner David R. Gunter	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The examiner notes that the "Power of Attorney by Assignee" statement included in the application was not signed.

2. The examiner acknowledges the applicant's claim to priority for the instant application as a continuation of application 08/934,097, filed 09/19/1997.

Specification

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The method steps of claims 1-15 lack antecedent basis in the preamble to claim 1. The preamble of Claim 1 recites the function "a method for determination of structure," but the method steps result in detection and quantification of the probe/folded DNA complex and not determination of the structure of the target DNA sequence.

b. The method steps of claims 16-20 lack antecedent basis in the preamble to claim 16. The preamble of Claim 16 recites the function "a method for analyzing the structure of nucleic acid targets," but the method steps result in immobilization of the probe/folded DNA complex and not analysis of the structure of the target DNA sequence.

c. The method steps of claims 21-28 lack antecedent basis in the preamble to claim 21. The preamble of Claim 21 recites the function "a method for analyzing folded nucleic acid targets," but the method steps result in immobilization of the probe/folded DNA complex and not analysis of the target DNA sequence.

d. The term "testing zones" in claim 16(a)(iv) and claim 21(a)(iii) is *non sequitur* to the claim as a whole and has no recited relationship to the previous steps of the corresponding claims. Addition of language that clarifies the relationship between the testing zones and the method is deemed necessary.

e. The term "substantially" in claims 17 and 24 is a relative term that renders the claim indefinite. Page 13, lines 3-5 of the specification states that "...while it is not necessary that absolutely no formation of the first probe/second folded target complex occurs, very little of this complex is formed." This definition in the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The applicant

should either define the hybridization conditions under which the method is to be performed and set limits for the acceptable level of hybridization for the first probed/second folded target complex, or remove the word "substantially" from the claims.

5. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. As stated above, the preambles to claims 1, 16, and 21 recite the functions of determining (claim1) and analyzing (claims 16 and 21) the structure of nucleic acid targets. The first sentence in the summary of invention (page 8, lines 13-15) states "[t]he present invention relates to methods and compositions for treating nucleic acids, and in particular, methods and compositions for detection and characterization of nucleic acid sequences and sequence changes." Several passages within the specification, for example page 32, lines 18-21, describe the generation of "a characteristic and reproducible pattern of complex formation for a given nucleic acid target, a characteristic 'fingerprint'" to be used for "identification of mutant forms of a target nucleic acid molecule." The passage found on page 39, line 25 through page 40, line 5, describes in detail a variety of formats in which this "hybridization signature of the conformation" can be analyzed and displayed.

The specification clearly demonstrates the critical and essential nature of developing a hybridization pattern or fingerprint in analyzing the structure of the target nucleic acid molecule. However, the method steps of claims 1-28 recite only formation, capture (immobilization), and quantification of a probe/DNA complex. Addition to the claims of the method step or steps

involved in determining and analyzing the structure of the target DNA based on formation, capture and quantification of the probe/DNA complex is deemed necessary.

Obviousness-type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1 of U.S. Patent No. 6,214,545 in view of USPN 6,355,437.

a. Claim 1 of the instant application recites a method for determining the structure of nucleic acid targets by combining a folded DNA target with one or more bridging oligonucleotide probes. Claim 1 of USPN 545 recites a method for combining a folded DNA target with "a plurality of different oligonucleotide probes." The method recited in UPSN 545 includes all of the method steps recited in Claim 1 of the instant application, but does not specifically address the types of probes to be used or how they interact with the target DNA. USPN 437 discloses a method similar to that disclosed in USPN 545 and the instant application, in which a folded DNA target is combined with "one or more bridging oligonucleotide probes" (column 13, line 10) with the purpose of "analyzing the structure of nucleic acid targets" (column 16, lines 1-2). It would have been obvious to one of ordinary skill in the art to modify the method recited in Claim 1 of USPN 545 to include the bridging oligonucleotide probes disclosed in USPN 437 in order to allow determination of the structure of the target folded DNA molecule.

b. Claim 2 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over USPN 545 in view of USPN 437. Claim 2 of the instant application recites a further limitation on Claim 1 that one or more of the intervening regions between the two non-contiguous target regions of the DNA target is at least five nucleotides in length. As described above, the claims of USPN 545 recite methods of forming a probe/folded DNA target complex, and USPN 437 discloses modifications to the method. In addition, the intervening region between non-contiguous target regions of the folded DNA target molecule in USPN 437 is disclosed in the specification as being at least five nucleotides in length (column 13, lines 16-18).

c. Claims 6-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over USPN 545 in view of USPN 437. Claims 6-15 in the instant application recite further limitations of Claim1 regarding capture of the probe/folded DNA complex using a moiety such as biotin incorporated into either the target or the oligonucleotide probe, which can subsequently be immobilized on a solid support. As described above, the claims of USPN 545 recite methods of forming a probe/folded DNA target complex, and USPN 437 discloses modifications to the method. All of the limitations recited in claims 6-15 of the instant application are also recited in claims 3-12 of USPN 545. Claims 6-15 of the instant application and claims 3-12 of USPN 545 depend upon independent claims that are slightly different, but clearly related as described above. The subject matter of Claims 3-12 of USPN 545 and the subject matter of Claims 6-15 in the instant application are identical. For this reason, Claims 3-12 of USPN 545 and Claims 6-15 in the instant application are not considered patentably distinct.

7. Claims 1 and 3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 437. Claim 1 of USPN 437 recites a method for detecting the presence of a target nucleic acid in a sample. The methods steps recited in Claim 1 of USPN 437 include all of the steps recited in Claim 1 of the instant application, and also includes a recitation of a method step for the detection of the probe/DNA complex as recited in claim 3 of the instant application. Based on the specificity of the oligonucleotide probes, it would have been obvious to one of ordinary skill in the art that the act

of detecting the complex formed by the target DNA and the bridging oligonucleotide (Claim 1, USPN 437) inherently determines the structure of the target DNA molecule (Claim 1, the instant application). Target DNA molecules that lack the expected structure will not bind to the bridging oligonucleotides and will thus escape detection. Only those molecules that have the expected structure can be detected.

8. Claims 16-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of USPN 6,210,880. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 of USPN 880 recites each of the individual steps listed in Claim 16 of the instant application. Claim 16 of the instant application recites a method in which bridging oligonucleotides are captured and immobilized on a solid support with a number of "testing zones". USPN 880 Claim 1 recites a method of "capturing" oligonucleotides using a solid support with a number of "capture zones". It would have been obvious to one of ordinary skill in the art that the "testing zones" of the instant application were the same as the "capture zones" of USPN 880. Claim 1, USPN 880 inherently determines the structure of the target DNA molecule as in Claim 16, the instant application because target DNA molecules that lack the expected structure will not bind to the bridging oligonucleotides and will thus escape capture. Only those molecules that have the expected structure can be captured and quantified.

9. Claims 21-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-13 of USPN 880. Although the conflicting

claims are not identical, they are not patentably distinct from each other because Claim 6 of USPN 880 recites each of the individual steps listed in Claim 21 of the instant application. The preamble of Claim 21 of the instant application recites a method for "analyzing folded nucleic acid targets," while the preamble of Claim 6 of USPN 880 recites a method for "forming a probe/folded target complex." Based on the specificity of the bridging oligonucleotide probes, it would have been obvious to one of ordinary skill in the art that the act of forming a complex of target DNA and the bridging oligonucleotide (Claim 6, USPN 880) inherently includes an analysis of the structure of the target DNA molecule (Claim 21, the instant application). Target DNA molecules that lack the expected structure will not bind to the bridging oligonucleotides and will thus not form the desired complex. Only those molecules that have the expected structure can bind the bridging oligonucleotide and form the desired complex.

Provisional Obviousness-type Double Patenting

10. Claims 1-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of co-pending Application No. 09/676,768 in view of USPN 437. Claims 1-14 of co-pending application 768 recite a process by which a folded DNA sequence is combined with one or more oligonucleotide probes that form a probe/folded target complex. The methods recited in Claims 1-14 of co-pending application 768 for detecting, quantifying, capturing, and labeling the probe/folded target complex are identical to those of Claims 1-15 of the instant application, as is the use of a probe attached to a solid support. Co-pending application 768 does not specifically teach that the DNA target contains an intervening region between two non-contiguous target regions, and does

not teach that the oligonucleotide probe to be used bridges this intervening region. USPN 437 discloses a method similar to that claimed in co-pending application 768 and the instant application, in which a folded DNA target is combined with "one or more bridging oligonucleotide probes" (column 13, line 10) with the purpose of "analyzing the structure of nucleic acid targets" (column 16, lines 1-2). It would have been obvious to one of ordinary skill in the art to modify the method recited in Claim 1 of co-pending application 768 to include the bridging oligonucleotide probes disclosed in USPN 437 in order to allow determination of the structure of the target folded DNA molecule.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 16-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15-27 of co-pending Application No. 768 in view of USPN 880. Claims 16-28 of the instant application recite methods for the analysis of nucleic acid targets using bridging oligonucleotides. Claims 15-27 of co-pending application 768 recite a process by which two folded DNA targets are combined with two oligonucleotide probes which form probe/folded target complexes. Co-pending application 768 does not specifically recite that the oligonucleotide probe to be used are bridging oligonucleotides. USPN 880 recites a method similar to that recited in co-pending application 768 and the instant application, in which folded DNA targets are combined with "bridging oligonucleotide probes." It would have been obvious to one of ordinary skill in the art to modify the method described in Claim 1 of co-pending application 768 to include the bridging

oligonucleotide probes disclosed in USPN 880 in order to broaden the range of potential probe/folded DNA target complexes which could be formed and captured.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David R. Gunter whose telephone number is (703) 308-1701. The examiner can normally be reached on 9:00 - 5:00 M - F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-9212 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

David R. Gunter, DVM, PhD
May 16, 2002

S. Elliott
SUPERVISORY PATENT EXAMINER
PRIMARY EXAMINER